

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Hsuan-Yin Lan-Hargest *et al.* Art Unit : Unknown  
 Serial No. : Unknown Examiner : Unknown  
 Filed : Herewith  
 Title : HISTONE DEACETYLASE INHIBITORS

# 3/10/00  
 3/9/00

Commissioner for Patents  
 Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the specification:

Please insert the following paragraph at page 1, line 2:

--This application is a continuation of U.S. Patent Application Serial No. 09/812,940, filed on March 27, 2001, the entire contents of which are hereby incorporated by reference.--

Please replace the paragraph beginning at page 1, line 13 with the following rewritten paragraph:

--Regulation of gene expression through the inhibition of the nuclear enzyme histone deacetylase (HDAC) is one of several possible regulatory mechanisms whereby chromatin activity can be affected. The dynamic homeostasis of the nuclear acetylation of histones can be regulated by the opposing activity of the enzymes histone acetyl transferase (HAT) and histone deacetylase (HDAC). Transcriptionally silent chromatin can be characterized by nucleosomes with low levels of acetylated histones. Acetylation of histones reduces its positive charge, thereby expanding the structure of the nucleosome and facilitating the interaction of transcription factors to the DNA. Removal of the acetyl group restores the positive charge condensing the structure of the nucleosome. Acetylation of histone-DNA activates transcription of DNA's message, an enhancement of gene expression. Histone deacetylase can reverse the process and can serve to repress gene expression. See, for example, Grunstein, *Nature* 389, 349-352 (1997); Pazin et al., *Cell* 89, 325-328 (1997); Wade et al., *Trends Biochem. Sci.* 22, 128-132 (1997); and Wolffe, *Science* 272, 371-372 (1996).--

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